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Lorazepam vs Midazolam for Acute Agitation

Introduction

1. Benzodiazepines are used for numerous acute states in the emergency department, especially agitation
2. IV access is often not available for patients with agitation and alternative routes must be considered; the drug of choice may change depending on the route of administration
3. This handout will focus on the pharmacokinetics of the two most utilized benzodiazepines in the emergency department, lorazepam and midazolam for acute agitation.

Pharmacology

	Lorazepam		Midazolam		
Administration	**IV**	**IM**	**IV**	**IM**	**IN**
Dose*	Sedation: 0.5-2 mg	Sedation: 0.5-2mg	Sedation: 0.5-2mg	Sedation: 2.5-5mg	Sedation: 0.1mg/kg
Onset	2-10 min (longer for anticonvulsant)	20-30 min	3-5 min	5-15 min	10 min
Duration	3 – 6 hours for seizures, up to 8 hours for sedation	6 – 8 hours	< 2 hour	1-2 hour	20-30 min
Bioavailability	100%	83-100%	100%	90%	44%
Pros /Cons	**Pro:** Fastest onset	**Pro:** No IV access needed **Con:** erratic absorption	**Con:** short duration, potential for recurrence of agitation/seizure	**Pro:** No IV access needed	**Pro:** Least invasive administration **Con:** small volumes (max 1mL each nare), high concentration drug needed
Concentrations available	2mg/mL	2mg/mL	1mg/mL 5mg/mL	1mg/mL 5mg/mL	5mg/mL

* typical anxiolytic dose. Other patients and conditions (alcohol withdrawal, sympathomimetic use) may require higher doses

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Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
Klein 2018	Prospective observational study N=737	• IM haloperidol 5 mg • IM ziprasidone 20 mg • IM olanzapine 10 mg • IM midazolam 5 mg • IM haloperidol 10 mg	At **15 minutes, midazolam resulted in a greater proportion of patients adequately sedated** (Altered Mental Status Scale <1) compared with all other drugs
Martel, 2005	Prospective, double-blind, randomized N=201	• IM droperidol 5 mg • IM midazolam 5 mg • IM ziprasidone 20 mg	**Adequate sedation was achieved at 15 minutes in patients receiving midazolam** compared to 30 minutes for droperidol and ziprasidone There was no difference in respiratory depression that clinically required treatment with supplemental oxygen
Nobay 2004	Prospective, double-blind, randomized N=95	• IM midazolam 5 mg • IM haloperidol 5 mg • IM lorazepam 2 mg	Mean time to sedation (min) **Lorazepam: 32.3 (±20)** **Midazolam: 18.3 (±14)** Haloperidol: 28.3 (±25) *lorazepam dropped from study due to significantly longer time to sedation and awakening
Meehan, 2001	Prospective, double-blind, randomized N=201	• IM olanzapine 10 mg • IM lorazepam 2mg • Placebo	At 2 hours, **olanzapine significantly greater reduction in scores on all agitation scales** compared with patients treated with either placebo or lorazepam
Battaglia 1997	Prospective, double-blind, randomized N=98	• IM haloperidol 5 mg • IM lorazepam 2 mg • IM haloperidol + lorazepam	Patient who received **combination treatment showed significantly greater reduction in symptoms compared to those receiving lorazepam** • No significant difference from haloperidol group
Wyant 1990	Observational N=15	• IM midazolam 5 mg • IM haloperidol 10 mg • IM sodium amytal 250 mg	**Midazolam was significantly more effective than haloperidol in controlling motor agitation**

Conclusions

1. Midazolam's quick onset, reliable IM absorption, and evidence that supports its use an effective pharmacologic agent for acute agitation could lead clinicians to argue that midazolam is more efficacious than lorazepam for acute agitation.

References

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